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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/966,881 | 09/28/2001 | Colin Roger Bird | 109846-288; SYN-106CON | 7251 |
| 23483 | 7590 | 07/30/2003 | EXAMINER | |
| HALE AND DORR, LLP 60 STATE STREET BOSTON, MA 02109 | | | KALLIS, RUSSELL | |
| ART UNIT | PAPER NUMBER | | | |
| 1638 | | | | |
| DATE MAILED: 07/30/2003 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|----------------|--------------|--|
| Office Action Summary | Applicant No. | Applicant(s) | |
| | 09/966,881 | BIRD ET AL. | |
| | Examiner | Art Unit | |
| | Russell Kallis | 1638 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 06 June 2003.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-18 is/are pending in the application.

 4a) Of the above claim(s) 12 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-11 and 13-18 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All- b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-14 are pending. Claims 15-18 are newly added and will be examined to the extent they read upon the elected sequence. Claims 1-11 and 13-18 are examined.

Claim Objections

Claims 1, 3, 5, 8, 11, 14, 16, and 17 are objected to because of the following informalities: At Claim 1, line 3, "at least one polynucleotide sequence selected from the sequences depicted as SEQ ID Nos 1-57" should be changed to reflect the election of SEQ ID NO: 13. The claim should read --the polynucleotide of SEQ NO: 13--. Further, throughout the claims, (Claims 1, 3, 5, 8, 11, 14, 16, and 17) where "at least one of the polynucleotides as claimed" or "at least one of the polynucleotide sequences described" or "at least one of the sequences depicted in the sequence listings as" should be changed to reflect the election of SEQ ID NO: 13. Appropriate correction is required.

Election/Restrictions

Applicant's election without traverse of Group I and SEQ ID NO: 13 in Paper No. 7 is acknowledged. The Claims will be examined to the extent they read upon the elected sequence. Applicant's request for reinclusion of SEQ ID NO: 14-17 and 18 because they all relate to pectate lyases is unpersuasive because there is nothing in Applicant's traversal or in the specification teaching that SEQ ID NO: 14-17 and 18 are structurally or functionally the same as SEQ ID NO: 13.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 7 and 15-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims modulation of ripening in the genus *Musa* transformed with a cDNA fragment obtained by hybridization with SEQ ID NO: 13 from a banana ripening cDNA library.

Applicant describes SEQ ID NO: 13.

Applicant does not describe fragments of SEQ ID NO: 13.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

Based upon the disclosure of SEQ ID NO: 13, there is insufficient relevant identifying characteristics to allow one skilled in the art to completely determine the structure of nucleic acid fragments of SEQ ID NO: 13, other than SEQ ID NO: 13, that modulate fruit ripening, absent further guidance. Since the claimed genus encompasses undisclosed or yet to be discovered sequences that modulate fruit ripening, the disclosure of SEQ ID NO: 1 does not provide adequate description of the claimed genus. In view of the level of knowledge and skill in the art one skilled in the art would not recognize from Applicant's disclosure that Applicant was in possession of nucleic acid fragments SEQ ID NO: 13, other than SEQ ID NO: 1, that modulate fruit ripening as broadly claimed.

Given the failure of a nucleic acid fragment of SEQ ID NO: 13 to be adequately described wherein fruit ripening is modulated, methods of its use are also inadequately described. See Written Description Guidelines, Federal Register Vol. 66 No. 4, Friday January 5, 2001 "Notices", pages 1099-1111.

Claims 1-11 and 13-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant broadly claims modulation of ripening in the genus *Musa* transformed with SEQ ID NO: 13. Modulation encompasses increasing ripening times, decreasing ripening times, reversing ripening process, and changes in the chemical makeup of compounds involved in the ripening process.

Applicant teaches prophetically the transformation and regeneration of *Musa* with a fruit ripening cDNA.

Applicant does not teach modulating fruit ripening with a fruit ripening cDNA in the genus *Musa*.

The phenotypic character expected from expression of a DNA construct often cannot be reliably predicted. In an example that demonstrates this all too common and unpredictable feature in the art, antisense expression of a polygalacturonase gene in transgenic tomato had no effect on fruit softening (Smith C. *et al.*, Nature 1988, 334: 724-726, p. 725).

Further, the lack of understanding of the complex mechanisms that regulate plant processes such as fruit ripening is characterized in experiments where transgenic plants designed to have an increased amount of lysine were limited in their accumulation of the amino acid because of increased lysine breakdown even though the flux through the pathway had increased, thereby suggesting that there are unforeseen mechanisms regulating plant processes that are not easily manipulated. Moreover, fruit ripening is a complex process governed by more than one enzyme and possibly more than one isoform of a ripening enzyme which may also be controlled at the transcriptional level. (Broun P. *et al.*, PNAS 2001, Vol. 98, no. 16, pp. 8925-8927; page 8926 column 2 lines 40-47 and the entire column 3).

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Given the unpredictability in the art engineering of fruit ripening; the breadth of the claims encompassing modulating ripening or tissue senescence; the lack of guidance in the examples of the specification or in the prior art for a method of modulating some unspecified quality or aspect of fruit ripening; although one of skill in the art can readily transform banana and plantain one would not know based upon Applicant's disclosure which embodiments would be inoperable and predictably eliminated, and thus undue trial and error experimentation would be needed by one skilled in the art to make a multitude of non-exemplified transformed plants from the genus *Musa* comprising SEQ ID NO: 13 to modulate in some unspecified manner the ripening phenotype in a multitude of non-exemplified transformed and regenerated *Musa* species. Therefore, the invention is not enabled.

With regard to Claims 3, 7 and 15-18, comprising a fragment that encompasses a single base of SEQ ID NO: 113.

Applicant broadly claims modulation of ripening in the genus *Musa* transformed with a cDNA fragment obtained by hybridization with SEQ ID NO: 13 from a banana ripening cDNA library.

Antisense inhibition of gene expression in transgenic plants using partial gene fragments is highly unpredictable. For example, expression of three constructs from different sections of one cDNA resulted in tissue specific reduction and increases of cDNA expression that varied with both construct and insertion event (Robbins M. *et al.* Plant Physiol., 1998; Vol. 116: 1133-1144; page 1139 column 2, lines 5-8 and page 1143 column 1, lines 1-30). The 3' half of an antisense cDNA construct was more effective than the 5' half in inhibition of flower pigmentation by antisense CHS genes (van der Krol A. *et al.*, Plant Molecular Biology, 1990;

Vol. 14: 457-466; page 460 column 1, lines 7-14 and column 2, lines 1-8). Further, variants of sense constructs were expected to co-suppress an endogenous nitrite reductase gene in transgenic tobacco but did not yield the expected phenotype (Crete P. *et al.* Plant Mol Biol 1999 Sep; 41(1):105-114; Abstract, lines 1-7).

Given the unpredictability in the art engineering of fruit ripening; the breadth of the claims encompassing modulating ripening or tissue senescence with a gene fragment of unspecified length; the lack of guidance in the examples of the specification or in the prior art for a method of modulating some unspecified quality or aspect of fruit ripening; although one of skill in the art can readily transform banana and plantain one would not know based upon Applicant's disclosure which embodiments would be inoperable and predictably eliminated, and thus undue trial and error experimentation would be needed by one skilled in the art to make a multitude of non-exemplified transformed plants from the genus *Musa* comprising some unspecified fragment that hybridizes to SEQ ID NO: 13 to modulate in some unspecified manner the ripening phenotype in a multitude of non-exemplified transformed and regenerated *Musa* species. Therefore, the invention is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 13-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At Claim 1, line 1 and line 5, "modulating" is indefinite. There is no comparative basis for modulation and it is unclear whether the modulation of ripening or senescence is to be

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accelerated or decelerated or if some other quality of the stated processes are to be changed such as coloring or sweetness or firmness. Further, the claim does not recite whether the property to be modulated is changed relative to some known standard.

Claim 1 and 3 are indefinite method claims because they are missing an expression step.

At Claim 3, line 1 and line 9, "modulating" is indefinite. There is no comparative basis for modulation and it is unclear whether the modulation of ripening or senescence is to be accelerated or decelerated or if some other quality of the stated processes are to be changed such as coloring or sweetness or firmness. Further, the claim does not recite whether the property to be modulated is modulated relative to some known standard or basis.

At Claim 3, lines 5-7, "0.3 strength citrate buffer" is indefinite. Strength is a relative term. Strength could refer to any number of properties of a solution such as molarity or weight of solute per volume of solvent (i.e. w/v) or percentage. Applicant should use standard notation when reciting buffer conditions.

At Claim 3, line 6, from 60 degrees C to 65 degrees C is indefinite. It is not clear whether Applicant intends to increase the temperature over the course of hybridization, or is intends that the range of hybridization can be between 60 to 65 degrees C.

At Claim 4, line 2, "modulates" is indefinite. There is no comparative basis for modulation and it is also unclear what property Applicant intends to modulate such as the timing of pectate lyase production, the amount of total pectate lyase produced, both, or some other property of pepctate lyase production.

At Claim 6, a method claiming a method is indefinite. It is unclear which method is desired.

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At Claim 7, "in claims 1 to 6" is indefinite. It is unclear which method is desired. The claim should read --in any one of Claims 1 to 6--.

At Claim 9, line 2, "switchable" is indefinite. It is unclear if the promoter that is "switchable" could be exchanged for another promoter or is capable of being induced chemically or by another gene product or is switchable between constitutive or developmental regulation.

At Claim 13, line 1, "associated" is indefinite because it does not disclose whether the association is directly related to fruit ripening or comprises properties tangential to fruit ripening.

At Claim 14, line 1, "retarded ripening phenotype" is indefinite. There is no comparative basis for this comparison.

At Claim 15, line 2, "modulates" is indefinite. The claim does not recite any comparative basis for production of pectate lyase.

Claims 1-18 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a method of modulating fruit ripening in banana and plantain transformed with an isolated polynucleotide of SEQ ID NO: 13.

All dependent claims recite "A" at the beginning. This should be changed to --The--.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 7 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed inventions encompass untransformed plants and seeds and the unspecified "material obtained from said plants" that may or may not have the transforming DNA, all of which read upon a product of nature and not one of the five classes of patentable subject matter. Claim 7 is drawn to parts such as seeds and progeny of the transformed plant. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be transferred at most to half the male gametes and half the female gametes. This translates into only two thirds of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Since the claim encompasses progeny that lack the transgene, the claim encompasses plants and seeds that are indistinguishable from plants and seeds that would occur in nature. See *American Wood v. Fiber Distintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Russell Kallis
July 28, 2003


PHUONG T. BUI
PRIMARY EXAMINER